20. (New) The method of claim 1, wherein said therapeutically-effective amount is from 20 mg/kg/day to 2500 mg/kg/day.

21. (New) The method of claim 1, wherein the compound of Formula IV is phenylacetic acid, a pharmaceutically acceptable salt of phenylacetic acid, or mixtures thereof.

22. (New) The method of claim 1, wherein the compound of Formula I is phenylacetylglutamine, a pharmaceutically acceptable salt of phenylacetylglutamine, or mixtures thereof.

23. (New) The method of claim 1, wherein the compound of Formula III is phenylacetylisoglutamine, a pharmaceutically acceptable salt of phenylacetylisoglutamine, or mixtures thereof.--

REMARKS

I. Status of the claims and support for the amendment

Claims 5-7 and 9-15, 17 and 18 are canceled

Claim 1 is amended and claims 19-23 are new.

Claims 1-4, 8, 16, and 19-23 are pending, a clean copy of all currently pending claims is attached hereto.

New claim 19 is directed specifically to the elected species, whereas new claims 20-23 are generic for, and read on, the elected species. Notwithstanding the fact that claim 16 does not read on the elected species, Applicant believes that claim 16 will be allowable once the other pending claims are allowed.

Support for the amendment of the claims is found in the claims as originally filed

II. Rejection under 35 U.S.C. § 103(a)

Claims 1-4 and 8 are rejected as allegedly being unpatentable over Applicant's admissions, regarding the prior art, at pages 2-3 of the specification, in view of Hendry *et al.* (U.S. Pat. No. 5,238,947, hereinafter "Hendry").

In making the rejection, the Examiner first points to page 3 lines 18-22 the instant specification which recites that:

> [i]t has been known for some time that compounds such as 3-phenylacetylamino-2,6-piperidinedione and its hydrolysis products, such as phenylacetic acid, and salts, precursors, and analogs thereof (together, "3-phenylacetylamino-2,6-piperidinedione and its derivatives"), can block the formation of iso-pentenylpyrophsphate from 5-pyrophosphomevalonate, a reaction in the pathway of cholesterol biosynthessis.

The Examiner next cites Hendry, which recites that:

> [t]he initial hydrolysis product and biological degradation product of A10 is phenylacetylglutamine, which is produced in vivo from phenylacetic acid and glutamine. In fact, A10 may be cyclized from phenylacetylactylglutamine in vivo.

(Hendry *et al.* column 2, lines 40-43). The Examiner then alleges that one of ordinary skill in the art would have been motivated to combine these teachings to provide the instantly claimed invention. Applicant respectfully traverses.

Applicant wishes to point out that the specification merely indicates that it was known that "3-phenylacetylamino-2,6-piperidinedione and its derivatives" can block a specific step in the cholesterol biosynthetic pathway (*i.e.* the synthesis of iso-pentenylpyrophosphate from 5-pyrophosphomevolonate). Applicant asserts that this is only to be interpreted as meaning that these compounds have been shown to block this specific enzymatic activity *in vitro*. There is nothing in the cited art to teach or suggest that "3-phenylacetylamino-2,6-piperidinedione and its derivatives" have the ability to block this enzymatic step *in vivo*. Furthermore, even if these compounds were known to able to function, *in vivo*, to inhibit the enzyme(s) responsible for the

conversion of 5-pyrophosphomevalonate to iso-pentenylpyrophsphate, this, alone, is not evidence that such inhibition would result in reduced serum cholesterol levels in affected patients. The fact that these compounds can reduce serum cholesterol levels *in vivo* was known only to the Applicant and was discovered as a consequence of the Applicant's own research, which resulted in the instant invention.

The MPEP provides that the following criteria which must be met in order to establish obviousness:

> To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (emphasis added).

MPEP 706.02(j) (emphasis added). Applicant asserts that there is nothing in the combination of the passages cited by the Examiner which renders the instant claims obvious by the standard of *In re Vaeck*. In particular, Applicant contends that the combination of art cited provides no reasonable expectation of success, *i.e.*, efficacious treatment of patients afflicted with hypercholesterolemia or hypertriglyceridemia.

Applicant believes that, with respect to the patentability of the instantly claimed invention, at worst, the combination of art cited by the Examiner could be construed as providing motivation to try to provide the claimed invention (Applicant does not, however, concede this point). Nevertheless, even if the Examiner concludes these passages would motivate a skilled artisan to try to provide the claimed invention, this is still not sufficient to establish a *prima facie*

case of obviousness. In the ruling of *In re Lindell,* 155 USPQ 521 (C.C.P.A. 1967) the court emphasized that:

> we have criticized the "obvious to try" test on several recent occasions....
>
> Furthermore, application of the "obvious to try" test would often deny patent protection to inventions growing out of well-planned research which is, of course, guided into those areas in which success is deemed most likely. These are, perhaps, the obvious areas to try. But resulting inventions are not necessarily obvious. Serendipity is not a prerequisite to patentability. Our view is that "obvious to try" is not a sufficiently discriminatory test.

Id., at 523.

Applicant asserts that the reasoning above has established that, at most, the passages cited by the Examiner, when combined, provide motivation to <u>try</u> to produce the claimed invention. The combination of these passages does not, in any way, make the claimed invention "obvious to succeed." Consequently, Applicant believes that the rejection of claims 1-4 and 8 under 35 U.S.C. § 103(a) has been overcome and respectfully request that this rejection be withdrawn.

III. Conclusion

In view of the above arguments, Applicant believes that claims 1-4, 8, 16, and 19-23 are now in condition for allowance.

The Examiner is invited to contact the undersigned patent agent at (713) 787-1589 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

Matthew Madsen

Matthew L. Madsen
Reg. No. 45,594
Agent for Applicant

HOWREY SIMON ARNOLD & WHITE, LLP
750 Bering Drive
Houston, Texas 77057-2198
(713) 787-1400

Date: 24 April 2001